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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/887,540	06/21/2001	Robert Klein	R-193	5814

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EXAMINER	
WILSON, MICHAEL C	

ART UNIT	PAPER NUMBER
1632	

DATE MAILED: 05/18/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/887,540	KLEIN, ROBERT	
	Examiner	Art Unit	
	Michael C. Wilson	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *27 February 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-4,13-19 and 24* is/are pending in the application.

4a) Of the above claim(s) *1-4 and 13-16* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *17-19 and 24* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

This application contains claims 1-4 and 13-16 drawn to an invention nonelected with traverse in Paper No. 10. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

Claims 20-23 and 25 have been cancelled. Claims 17-19 and 24 remain under consideration in the instant office action.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Applicant's arguments filed 2-27-04 have been fully considered but they are not persuasive.

Claim Objections

LRP5 should be clearly set forth in all independent claims as "low density lipoprotein-related protein 5 (LRP5)" first. It may then be referred to as LRP5 thereafter within the claim and in dependent claims.

Claim Rejections - 35 USC § 101

Claims 17-19 and 24 remain rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific or substantial asserted utility or a well-established utility.

Claims 17-19 are directed toward a transgenic animal having a disruption of an LRP5 gene and retinal degeneration, increased anxiety or hypoactivity. The

specification teaches making LRP5 -/- mice (pg 50). The specification suggests using the mice to test compounds for neurological, neuropsychological or psychotic disease, but the specification does not disclose one specific neurological, neuropsychological or psychotic disease in humans linked to a disruption in LRP5 (pg 19, lines 8-11). The mice were tested in "open field testing" (Fig. 4 and 5 and pg 51); however, the results of the open field test do not correlate to a useful phenotype because "possible increased anxiety" and "significant hypoactivity" (lines 4 and 7 of pg 51) are not specific to any disease and are not statistically significant because the number of mice tested is not disclosed and the difference observed is not significant. In fact, it cannot be determined what the "2,1," means in "2,1, -/-, Male" or "2,1, +/+, Male" in Fig. 4 and 5. The mice also had retinal degeneration. The specification suggests using the mice as a model of disease relating to disruptions in LRP5 (pg 19, lines 4-6). However, retinal degeneration has not been linked to the LRP5 gene in humans. The mice claimed cannot be used to determine compounds that modulate LRP5 expression because LRP5 is not expressed in the mice. Using the mice to determining whether a particular phenotype is ameliorated is not a specific or substantial utility because the specification does not link the phenotype to any specific disease or to a disease caused by a disruption in humans. The specification does not identify any compounds that alter neurological, neuropsychological, or psychotic phenotypes using the mice. Thus, the specification does not provide a specific or substantial use for a mouse having retinal degeneration, increased anxiety or hypoactivity as claimed.

Since the time of filing, LPR5 disruptions have been linked to osteoporosis-pseudoglioma syndrome (OPPG) in humans (Gong, 11-16-01, Cell, Vol. 107, pg 513-523, abstract), which is not taught or suggested in the instant application. A mouse having a homozygous disruption in LRP5 having features of osteoporosis-pseudoglioma syndrome has been made since the time of filing (Kato, J. Cell Biology, 2002, Vol.1 57, pg 303-314; abstract and pg 304, col. 2, "Generation of Lrp5-/- mice"), which is not taught or suggested in the instant application.

Claim 24 is included because it is directed toward making the mouse, which lacks utility for reasons above.

Applicants assert a link exists between retinal degeneration, increased anxiety and hypoactivity claimed and specific disease or disease caused by a disruption in humans. Applicants assert that such a link is generally accepted in the art of transgenic and knockout mice. Applicants' argument is not persuasive. No link between a disruption in LRP5 and retinal degeneration, increased anxiety and hypoactivity in humans exists. The only way such a link would be "generally accepted in the art of transgenics" would be if scientists determined that some humans with retinal degeneration, increased anxiety and hypoactivity had a disruption in the LPR5 gene. No humans with retinal degeneration, increased anxiety and hypoactivity have been determined to have a disruption in the LPR5 gene.

Applicants argue because the mouse and human gene are homologous, humans having a disruption in the LPR5 gene would also have retinal degeneration, increased anxiety and hypoactivity. Applicants' argument is not persuasive. The effect of a

disruption in LPR5 may affect mice differently than humans. The role of LPR5 may be different in mice than humans. The art at the time of filing is replete with examples of proteins that behave differently in mice and humans. Applicants have not linked a LPR5 gene disruption to any disease state in humans. Without such teachings, the mouse having a disruption of a LPR5 gene does not have utility because it does not reflect a known human condition.

Applicants argue the mice have uses for models for disease (pg 6 of response). These arguments are not persuasive because the mice do not reflect any human disease state, i.e. it has not been shown that a disruption in LPR5 causes retinal degeneration, increased anxiety or hypoactivity in humans.

Applicants argue the mice can be used to test for drugs that treat retinal degeneration, increased anxiety and hypoactivity. It cannot be determined how to test drugs for treating retinal degeneration, increased anxiety or hypoactivity in humans when a disruption LPR5 is not the cause of the retinal degeneration, increased anxiety or hypoactivity. Drugs found using a mouse having a disruption in LPR5 may not work if retinal degeneration, increased anxiety or hypoactivity was caused by some other means. Drugs found using mice having a disruption in LPR5 may be specific to disruptions in LPR5. if the disruption does not occur in humans, then the drugs would not function in humans. If a drug is found using the mouse claimed, and the drug is generic to retinal degeneration caused by any means, then the drug could have been found using any mature wild-type mouse that had retinal degeneration, and the drug would not be specific to a disruption in LPR5.

Claim Rejections - 35 USC § 112

Claims 17-19 and 24 remain rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific or substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use mice having retinal degeneration, increased anxiety or hypoactivity.

In addition, claims 17 and 24 do not provide a nexus between the disruption in LRP5 and the lack of production of LRP5 or the phenotypes of retinal degeneration, increased anxiety or hypoactivity.

Claim 17 is directed toward a transgenic mouse having a disruption in LRP5 that lacks production of functional low density LRP5, and exhibits retinal degeneration, increased anxiety, or hypoactivity. Claim 24 is directed toward a method of making a transgenic mouse having a disruption in LRP5 using a mouse ES cell having a disruption in an endogenous LRP5 gene, introducing the cell into a mouse blastocyst, implanting the blastocyst into a pseudopregnant mouse which gives birth to chimeric mice, and breeding the chimeric mouse to produce the transgenic mouse, wherein the disruption is homozygous, the mouse lacks production of functional low density LRP5, and has retinal degeneration, increased anxiety, or hypoactivity.

Applicants' arguments are addressed above in the utility rejection.

Claims 17-19 and 24 remain rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 17 and 24 remain rejected for reasons of record because it cannot be found where a mouse having a disruption in LRP5 also has hypoactivity (claims 17 and 24). A mouse having retinal degeneration as a result of a disruption in LRP5 can be found on pg 50, lines 19-30. The limitation of "increased anxiety" can be found on pg 51, lines 3-5.

Claims 17-19 and 24 remain rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The rejection of claims 17 and 24 relating to clearly setting forth that the disruption in LRP5 causes the lack of production of LRP5, retinal degeneration, increased anxiety or hypoactivity has been withdrawn in view of the amendments to the claims.

The rejection of claims 17 and 24 because "increased anxiety and hypoactivity" are relative terms has been withdrawn in view of the amendments to the claims.

The rejection of claims 18 and 19 because it is unclear whether the field test is related to the increased anxiety or hypoactivity in claim 17 or if it is in addition to the

increased anxiety or hypoactivity in claim 17 has been withdrawn because of the amendments to the claims.

The rejection regarding the term "characterized" in claims 18 and 19 has been withdrawn because the term has been deleted.

The rejection of claim 21 has been withdrawn because the claim has been cancelled.

The rejection regarding "increased anxiety" or "hypoactivity" in claims 22 and 23 has been withdrawn because the claims have been cancelled.

Claim Rejections - 35 USC § 102

The rejection of claim 20 under 35 U.S.C. 102(b) as being anticipated by Weaver (J. Biol. Chem., 1997, Vol. 272, pg 14372-14379) has been withdrawn because the claim has been cancelled.

Double Patenting

The objection to claim 25 under 37 CFR 1.75 as being a substantial duplicate of claim 17 has been withdrawn because claim 25 has been cancelled.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

No claim is allowed.

Inquiry concerning this communication or earlier communications from the examiner should be directed to Michael C. Wilson who can normally be reached on Monday through Friday from 9:00 am to 5:30 pm at 571-272-0738.

Questions of a general nature relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-1235.

If attempts to reach the examiner, patent analyst or Group receptionist are unsuccessful, the examiner's supervisor, Amy Nelson, can be reached on 571-272-0804.

The official fax number for this Group is (703) 872-9306.

Michael C. Wilson

MICHAEL WILSON
PRIMARY EXAMINER